

It is claimed:

1. A method of improving in a subject the pharmacokinetics of a drug, comprising co-administering with said drug a morpholino antisense oligomer effective to reduce synthesis of a drug-metabolizing cytochrome p450 enzyme that reduces the effectiveness of the drug, by hybridizing to a target RNA molecule which encodes said enzyme.
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2. The method of claim 1, wherein the drug either induces said drug-metabolizing cytochrome p450 enzyme, or is administered to a subject who has been exposed to a
10 xenobiotic agent which induces such an enzyme.
3. The method of claim 2, wherein said drug induces at least one cytochrome p450.
4. The method of claim 2, wherein said xenobiotic agent induces at least one cytochrome
15 p450.
5. The method of claim 1, wherein the antisense oligomer hybridizes to a region of the target RNA molecule which includes the AUG translation start site.
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6. The method of claim 1, wherein the target RNA molecule is pre-mRNA, and the antisense oligomer hybridizes to a region of the pre-mRNA which includes an intron-exon boundary or an exon-intron boundary.
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7. The method of claim 1, wherein the antisense oligomer is at least 15 nucleotides in length.
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8. The method of claim 1, wherein the antisense oligomer has an uncharged backbone comprising phosphoramidate or phosphorodiamidate linkages.
9. The method of claim 1, wherein the antisense oligomer hybridizes to a region of said target RNA with a T_m greater than 37°C.
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10. The method of claim 1, wherein the antisense oligomer is administered orally to the subject.
11. The method of claim 10, wherein said oligomer is administered in an amount of at least 1 mg/kg body weight.
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12. The method of claim 1, wherein the antisense oligomer is administered transdermally to the subject.

13. The method of claim 1, wherein said cytochrome p450 is selected from the group consisting of CYP1A1, CYP1A2, CYP2A6, CYP2B1, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A2, CYP3A4, and CYP6A1.

5 14. The method of claim 1, wherein said subject is a human subject, and said cytochrome p450 is selected from the group consisting of CYP1A1, CYP1A2, CYP2A6, CYP2B1, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4.

10 15. The method of claim 13, wherein said cytochrome p450 is selected from the group consisting of CYP1A2, CYP2B1, CYP2E1, and CYP3A4.

16. The method of claim 3, wherein said cytochrome p450 is CYP2E1, and said drug is acetaminophen.

15 17. The method of claim 3, wherein said cytochrome p450 is from the CYP2B or CYP3A subfamily, and said drug is phenobarbital or hexobarbital.

18. The method of claim 17, wherein said cytochrome p450 is CYP2B1.

20 19. The method of claim 3, wherein said cytochrome p450 is CYP3A4, and said drug is an antibiotic selected from the group consisting of clarithromycin, erythromycin, rifampicin, rifampin, rifabutin, and rapamycin.

25 20. The method of claim 3, wherein said cytochrome p450 is CYP3A4 or CYP1A2, and said drug contains an estrogen or estradiol.

21. The method of claim 4, wherein said cytochrome p450 is CYP3A4, said drug is a protease inhibitor or non-nucleoside reverse transcriptase inhibitor, and said xenobiotic is a CYP3A4-inducing non-nucleoside reverse transcriptase inhibitor.

30 22. The method of claim 1, wherein said oligonucleotide is selected from the group consisting of SEQ ID NOS: 16-35 and SEQ ID NO: 46-47.

35 23. The method of claim 22, wherein said oligomer is selected from the group consisting of SEQ ID NOS: 26-35 and SEQ ID NOS: 46-47.

24. The method of claim 23, wherein said oligomer is selected from the group consisting of SEQ ID NOS: 27, 30, 34, 35, and 46-47.